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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,840	03/15/2004	Gordon J. Dow	2102.010US2	1530

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
05/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,840	DOW ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2·6·07
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed February 6, 2007 have been entered.

Claims 45-64 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gordon (Clinical therapeutics, 1998; 20(1): 26-39) and Hill (WO 92/14472) in view of Richards (US Patent 4,985,418), and Budavari (Merck Index 11th ed. 1989, monograph 6021 and 7879) references of record in the parent application.

Gordon teaches a corticosteroid (clobetasol) containing composition, free of mineral oil and white soft paraffin, employing Cetostearyl alcohol, cetomacrogol 1000, Isopropyl myristate, propylene glycol, Dimethicone 360, citric acid, sodium citrate, imidurea, and water (see page 28, table 1). Gordon also teaches the function for adding occlusive agents in emollient cream will help moistening the skin (See page 32, col. 2). Gordon also teaches the absorption of the steroids is greater when more occlusive agents are present in the formulation (See page 32, col. 2).

Hill teaches a topical composition employing 0.05% of the corticosteroid, fluticasone propionate, 10.00% of cetostearyl alcohol, 10% of White Soft Paraffin,

2.50% of Polysorbate 60, 10.00% of propylene glycol, and purified water (see particularly Example 1). Hill also teaches that the topical composition is useful in treating skin conditions including inflammation (See particularly page 1, 6th paragraph).

The references do not expressly teach the composition with the specific amount of white paraffin. The references do not expressly teach the employment of methyl paraben and propyl paraben in the lotion. The references do not expressly teach the weight percentage of surfactant to be about 0.5 to 2.0%.

Richards teaches that methyl paraben and propyl paraben are excipients known to be useful in a fluticasone topical composition (See particular col. 5, lines 20-30). Richards also teaches the preparation of the fluticasone composition involving the process of mixing the ingredients at 70 degree Celsius and then heating the mixture to 70 degree (See particular col. 6, line 10-17).

Budavari teaches both methyl parabena and propyl paraben are useful as preservatives and pharmaceutic aids (See the Use section of the monographs).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to formulate a topical fluticasone composition as free of mineral oil and white soft paraffin with the ingredients herein in the amount herein. It would have also been obvious for one of ordinary skill in the art at the time the invention was made to prepare a topical fluticasone composition that has the herein claimed amount of surfactant.

One of ordinary skill in the art would have been motivated to formulate a topical fluticasone composition, as free of mineral oil and white soft paraffin, with the exicipient

ingredients in the amount herein. Possessing the teachings of the cited prior art, one of ordinary skill in the art would be reasonably expected to successfully substitute clobetasol with fluticasone to formulate an emollient cream up to 5% mineral oil and white soft paraffin (includes 0% of mineral oil and white paraffin). Furthermore, the excipients herein are known to be useful in formulating topical corticosteroid compositions. Therefore, incorporating all the excipients herein with any known active corticosteroid compounds including fluticasone would have been reasonably expected to be useful in preparing the topical fluticasone composition herein. Furthermore, the optimization of desired effect parameters (amount of excipients) is obvious as being within the skill of the artisan, absent evidence to the contrary.

Response to Arguments

Applicant's arguments filed February 6, 2007 averring the instant specification not including dimethicone as a skin conditioning agent have been fully considered but they are not persuasive. It is noted that the instant claim recites a skin conditioning agent broadly. It does not limit or exclude any skin conditioning agent from the claim. Since dimethicone can be served as a skin conditioning agent, the cited reference is seen to read on the claim.

Applicant's arguments filed February 6, 2007 averring claims 45-47 is patentable over the cited prior art because the cited prior arts do not teach a composition that is free of white paraffin or mineral oil, have been considered, but are not found persuasive. Examiner notes that Gordon's composition is free of mineral oil and paraffin. Possessing the teachings of the cited prior arts, one of ordinary skill in the art would

therefore substitute clobetasol with fluticasone to formulate an emollient cream free of mineral oil and white soft paraffin. With addition of the well-known auxiliary agents such as the preservatives for topical pharmaceutical composition, the composition suggested in the cited prior arts renders the instant invention obvious.

Applicant's arguments filed February 6, 2007 averring the cited prior art's failure to provide motivation to adjust the amount of dimethicone have been fully considered but they are not persuasive. Gordon provides the motivation of adding or adjusting the amount of the occlusive agents since it can affect the absorption of the steroid, and thus, its efficacy in the skin (i.e., affecting blanching scores). Therefore, it would be seen that one of ordinary skill in the art would be motivated to optimize the amount of dimethicone.

Applicant's arguments filed February 6, 2007 with regard to the potency of the different steroids and the diminished amount of occlusive agents have been considered, but are not found persuasive. As discussed above, the occlusive agents employed in Gordon can affect the efficacy of the steroids in the skin. In other words, the potency of the steroids can adjusted up or down depending on the indications and particular use. Although dimethicone is used in the instant invention as something other than occlusive agent for skin protection, dimethicone, according to Gordon, is served as occlusive agent. Therefore, it is not totally correct when the applicant characterizes the herein claimed composition as absent of any occlusive agents. Therefore, the alleged "unexpected" benefits can be due to the presence of dimethicone in the composition

serving as occlusive agent (See Gordon, page 28, Table I and page 30, col. 2, second paragraph).

Applicant's arguments filed February 6, 2007 with regard to the inclusion of dimethicone of Gordon into Hill composition have been considered, and are not found persuasive. Examiner notes that inlcluding dimethicone of Gordon into Hill's composition is never the motivation of the outstanding rejection under 35 USC 103(a). Therefore, such arguments are seen to be irrelevant to the obviousness rejection herein. The motivation to combine the cited prior arts, as discussed, is based on the substitution of clobetasol with fluticasone to formulate an emollient cream free of mineral oil and white soft paraffin would be obvious based on the teachings of the cited prior arts. Examiner notes that Gordon's composition has almost all of the components as claimed.

Applicant's arguments filed February 6, 2007 averring the presence of the unexpected results have been considered, but are not found persuasive. It is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In regard to any possible unexpected result

presented in the instant application, the specification, the data at pages 14-19 has been considered but not found persuasive as to the presence of unexpected result. The data in page 15, Table 1 demonstrates that the Lotion in Examples 1 and 2 apparently had a higher Area Under the Curve than that of Cutivate® cream. However, it is not clear as to the statistical error of the measurement. Further, it is unclear that Cutivate cream represents the closest prior art for evaluation of unexpected results by comparison. Therefore the data does not clearly and convincingly demonstrate unexpected results. The nature of the composition of Cutivate® cream demonstrated in the specification herein, e.g., ingredients and amount of each is unclear. Therefore, the relevance of the AUC difference in Table 1 determining unexpected results for the claimed invention over the closest prior art is unclear.

In regard to the data in page 16, Table 2, the AUC and the blanching score of the fluticasone lotion within the instant claims is apparently higher than Cutivate cream and Hytone™ lotion but is lower than the Temovate™ and Elocon™. However, the statistical error of the measurement is not presented. Therefore the data does not clearly and convincingly demonstrate unexpected results. Moreover, it is not clear that Cutivate® cream, Hytone lotion, Temovate, and Elocon represent the closest prior art for evaluation of unexpected results by comparison. The nature of the compositions of Cutivate® cream, Hytone lotion, Temovate, Elocon demonstrated in the specification herein, e.g., ingredients and amount of each is unclear. Therefore, the relevance of the AUC and blanching score difference in Table 2 on page 16 determining unexpected results for the claimed invention over the closest prior art is unclear.

The data presented in Table 3 of page 17 demonstrates the effectiveness of the fluticasone lotion within the claims in treating atopic dermatitis as compared to a placebo. It is seen to be an expected therapeutic result based on the cited prior art. The data in Table 4, page 18-19 demonstrates the safety of the employment of fluticasone lotion. Please note that the use of fluticasone lotion to achieve therapeutic effect is expected to be safe. No comparative data is present to evaluate the unexpected result. Moreover, it is not clear the amount of fluticasone lotion which was applied. It is not clear what the percentage of subjects using Cutivate cream experiencing side effects is. In addition, it is unclear that Cutivate cream represents the closest prior art for evaluation of unexpected results by comparison. Therefore no clear and convincing unexpected results are seen to be present herein.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1617